Bohring-Opitz syndrome

Bohring-Opitz syndrome is a rare condition that affects the development of many parts of the body.

People with Bohring-Opitz syndrome have abnormal development of the head. They often have a small head size (microcephaly) and a skull abnormality called trigonocephaly, which gives the forehead a pointed appearance. Brain abnormalities result in profound to severe intellectual disability and developmental delay in affected individuals. Many people with this condition experience seizures.

Characteristic eye problems occur in people with Bohring-Opitz syndrome. They may have protruding eyes (exophthalmos), eyes that do not point in the same direction (strabismus), widely spaced eyes (hypertelorism), or outside corners of the eyes that point upward (upslanting palpebral fissures). Affected individuals may have nearsightedness (myopia) or abnormalities in the light-sensitive tissue at the back of the eye (the retina) or the nerves that carry information from the eyes to the brain (optic nerves), which can impair vision.

Additional facial features of Bohring-Opitz syndrome can include a flat nasal bridge, nostrils that open to the front rather than downward (anteverted nares), a high arch or opening in the roof of the mouth (high arched or cleft palate), a small lower jaw (micrognathia), low-set ears that are rotated backward, a red birthmark called a port-wine stain on the forehead, and a low frontal hairline with excessive facial hair (hirsutism).

Individuals with Bohring-Opitz syndrome have poor growth before birth (intrauterine growth retardation). During infancy they experience a failure to gain weight and grow at the expected rate (failure to thrive) and often have feeding difficulties.

People with this condition often have characteristic positioning of the upper body, known as Bohring-Opitz syndrome posture. This posture consists of slouching shoulders, permanently bent elbows and wrists, and a hand deformity in which the wrist or all of the fingers are angled outward toward the fifth finger (ulnar deviation). Joint deformities called contractures in the knees, hips, or other joints that are apparent at birth and abnormal muscle tone may also occur in this condition. Affected individuals can have recurrent infections and heart, kidney, or genital abnormalities. In rare cases, a childhood form of kidney cancer known as Wilms tumor can develop.

Some individuals with Bohring-Opitz syndrome do not survive past early childhood, while others live into adolescence or early adulthood. The most common causes of death are recurrent episodes of an abnormally slow heartbeat (bradycardia), which eventually leads to a fatal lack of oxygen in the body's organs and tissues;

abnormalities of the throat and airways that cause short pauses in breathing (obstructive apnea); and lung infections.

Frequency

Bohring-Opitz syndrome is thought to be a rare condition, although its exact prevalence is unknown. More than 40 affected individuals have been described in the scientific literature.

Genetic Changes

Bohring-Opitz syndrome is caused by mutations in the *ASXL1* gene. This gene provides instructions for making a protein that is involved in a process known as chromatin remodeling. Chromatin is the complex of DNA and proteins that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Through its role in chromatin remodeling, the *ASXL1* gene regulates the activity (expression) of many genes, including a group of genes known as HOX genes, which play important roles in development before birth. The ASXL1 protein can turn on (activate) or turn off (repress) HOX genes depending on when they are needed.

It is unclear how *ASXL1* gene mutations cause the signs and symptoms of Bohring-Opitz syndrome. *ASXL1* gene mutations reduce the amount of functional ASXL1 protein available, which likely disrupts the regulation of the activity of HOX genes and other genes during development. Altered activity of these genes probably leads to the neurological and physical features of this condition.

Inheritance Pattern

Bohring-Opitz syndrome is considered an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of the condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family. Because the condition is so severe, no one with Bohring-Opitz syndrome has been known to have children.

Other Names for This Condition

- Bohring syndrome
- BOPS
- C-like syndrome
- Oberklaid-Danks syndrome
- Opitz trigonocephaly-like syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: C-like syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796232/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Failure to Thrive
  https://medlineplus.gov/ency/article/000991.htm
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html
- Health Topic: Eye Diseases
  https://medlineplus.gov/eyediseases.html

Genetic and Rare Diseases Information Center

- Bohring-Opitz syndrome
  https://rarediseases.info.nih.gov/diseases/10140/bohring-opitz-syndrome

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Microcephaly Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Microcephaly-Information-Page

Educational Resources

- Boston Children's Hospital: Metopic Synostosis (Trigonocephaly) Symptoms & Causes
  http://www.childrenshospital.org/conditions-and-treatments/conditions/m/metopic-synostosis-trigonocephaly/symptoms-and-causes
- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html
- Centers for Disease Control and Prevention: Facts About Microcephaly
  https://www.cdc.gov/ncbddd/birthdefects/microcephaly.html
- Disease InfoSearch: C-Like Syndrome
  http://www.diseaseinfosearch.org/C-Like+Syndrome/1011
- Johns Hopkins Medicine: Failure to Thrive
  http://www.hopkinsmedicine.org/healthlibrary/conditions/pediatrics/failure_to_thrive_90,P02297/
- KidsHealth from Nemours: Failure to Thrive
  http://kidshealth.org/en/parents/failure-thrive.html
- MalaCards: bohring-opitz syndrome
  http://www.malacards.org/card/bohring_opitz_syndrome
- Oregon Health Sciences University: Metopic Synostosis
  http://www.ohsu.edu/xd/health/services/doernbecher/programs-services/trigonocephaly.cfm
- Orphanet: Bohring-Opitz syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=97297

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  http://aaidd.org/
- Bohring-Opitz Syndrome Foundation
  http://bos-foundation.org/
- Children's Craniofacial Association
  http://www.ccakids.com/
- Cleft Palate Foundation
  http://www.cleftline.org/

- FACES: The National Craniofacial Association
  http://www.faces-cranio.org
- The Arc
  http://www.thearc.org/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Bohring-Opitz+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28Bohring-Opitz+syndrome%5BTIAB%5D%29+OR+%28C-like+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- BOHRING-OPITZ SYNDROME
  http://omim.org/entry/605039

Sources for This Summary

- Bohring A, Oudesluijs GG, Grange DK, Zampino G, Thierry P. New cases of Bohring-Opitz syndrome, update, and critical review of the literature. Am J Med Genet A. 2006 Jun 15;140(12): 1257-63. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16691589
- Hoischen A, van Bon BW, Rodríguez-Santiago B, Gilissen C, Vissers LE, de Vries P, Janssen I, van Lier B, Hastings R, Smithson SF, Newbury-Ecob R, Kjaergaard S, Goodship J, McGowan R, Bartholdi D, Rauch A, Peippo M, Cobben JM, Wieczorek D, Gillessen-Kaesbach G, Veltman JA, Brunner HG, de Vries BB. De novo nonsense mutations in ASXL1 cause Bohring-Opitz syndrome. Nat Genet. 2011 Jun 26;43(8):729-31. doi: 10.1038/ng.868.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21706002
- Magini P, Della Monica M, Uzielli ML, Mongelli P, Scarselli G, Gambineri E, Scarano G, Seri M. Two novel patients with Bohring-Opitz syndrome caused by de novo ASXL1 mutations. Am J Med Genet A. 2012 Apr;158A(4):917-21. doi: 10.1002/ajmg.a.35265. Epub 2012 Mar 14.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22419483
- Russell B, Johnston JJ, Biesecker LG, Kramer N, Pickart A, Rhead W, Tan WH, Brownstein CA, Kate Clarkson L, Dobson A, Rosenberg AZ, Vergano SA, Helm BM, Harrison RE, Graham JM Jr. Clinical management of patients with ASXL1 mutations and Bohring-Opitz syndrome, emphasizing the need for Wilms tumor surveillance. Am J Med Genet A. 2015 Sep;167A(9):2122-31. doi: 10.1002/ajmg.a.37131. Epub 2015 Apr 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25921057
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4760347/

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https://ghr.nlm.nih.gov/condition/bohring-opitz-syndrome

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